Remarks

Claims 1 and 8 to 35 are pending and before the Examiner. Applicants again point out that similar issues (e.g., concerning the enablement of "prevention" in the claims) are present and similar rejections have been made in copending U.S.S.N. 10/757,295, which is also being examined by the Examiner.

The Examiner rejected claims 1 and 8 to 17 as allegedly failing to provide enablement under 35 U.S.C. § 112, first paragraph, for the prevention of the recited conditions.

In response, applicants traverse the rejection of the claims directed to prevention as improper. "When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application; this includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement". *In re Wright*, 27 U.S.P.Q. 1510, 1513 (Fed. Cir. 1993)(emphasis added).

First, the Examiner states that metabolic syndrome is "complex", but does not explain why that causes any doubt as to the effectiveness of prevention of metabolic syndrome using the claimed method. Given that the claimed method of treating metabolic syndrome is enabled, it would follow that prevention is enabled even if metabolic syndrome is "complex". Again, the reasoning of *Ex parte Cho*, Appeal No. 2001-2646 (Bd. Pat. App. & Int. 2002)(nonprecedential) is particularly compelling for the instant claims which are directed to a discrete combination of two very well-known chemical entities. As the Board stated, "Logically, if the recited compounds are useful for treating conditions such as pain and inflammation once they exist, they would also be expected to be effective in preventing pain and inflammation, if they were administered before the onset of pain or inflammation." (emphasis in original) is a generalized statement not limited to the specific technology of *Ex parte Cho*. The Examiner concedes enablement of the instant claimed combination for treatment of the recited conditions, which would make the logical generalization of *In re Cho* even more obviously on point.

Second, although the Examiner states that "the instant rejection focuses on the particular condition of metabolic syndrome .... the reasons stated here apply also to myriad [*sic*] of other conditions encompassed by the present claims ...", the Examiner gives no reasoning supporting any rejection concerning preventing asthma, bronchitis, interstitial lung disease, insulin resistance, prediabetes, type 2 diabetes mellitus, metabolic syndrome, hypertension combined with hyperlipidaemia, or hypertension combined with atherosclerosis as recited in the claims. The Examiner has accordingly not met the burden of providing any reasoning concerning the rejection of this subject matter. Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

The Examiner also again rejected claims 1 and 8 to 35 as allegedly unpatentable under 35 U.S.C. § 103(a) over De Gasparo *et al.*, in light of Robl *et al.*, in view of Cecil's Textbook of Medicine (2000), Harlan *et al.* (U.S. Patent Appl. Pub. No. 2001/0006656), and Bohm *et al.* (WO 02/15891).

Applicants again respectfully traverse the rejection. De Gasparo *et al.* does not specifically disclose the specific combination of telmisartan and simvastatin anywhere, as the Examiner acknowledges. The teachings and statements in De Gasparo *et al.* must be considered in context and interpreted as a whole. De Gasparo *et al.* discloses a combination of angiotensin II receptor blockers and HMG-CoA reductase inhibitors, which in general encompasses, but does not teach or disclose, the combination of telmisartan and simvastatin. De Gasparo *et al.* does not disclose a specific technical teaching which would suggest to the person skilled in the art to select telmisartan from among the various sartans mentioned or even give any technical preference to one of the various combinations suggested. De Gasparo *et al.* thus generally offers the options of:

(a) AT_1 receptor antagonist + HMG-Co-A reductase inhibitor;
(b) AT_1 receptor antagonist + ACE inhibitor
(c) AT_1 receptor antagonist + HMG-Co-A reductase inhibitor + ACE inhibitor;
(d) AT_1 receptor antagonist + diuretic + HMG-Co-A reductase inhibitor;
(e) AT_1 receptor antagonist + diuretic + ACE inhibitor; and
(f) AT_1 receptor antagonist + diuretic + HMG-Co-A reductase inhibitor + ACE inhibitor.

In contrast, the present invention is based on three important selections for which there is no guidance in De Gasparo *et al.* First, the specific combination type of AT_1 receptor antagonist + HMG-Co-A reductase inhibitor is selected. Second, the selection of telmisartan as the AT_1 receptor antagonist, which is shown for the first time to have a uniquely strong effect on genes regulated by the PPARgamma receptor, a receptor which was known to the person skilled in the art to interfere with lipid and glucose metabolism is made. This unexpected effect of the specific AT_1 receptor antagonist telmisartan makes telmisartan a particularly preferred combination partner for lipid lowering HMG-Co-A reductase inhibitors. Third, the selection of simvastatin as the HMG-Co-A reductase inhibitor is made. Simvastatin shares with telmisartan lipophilic properties while representing an optimized natural (semi-synthethetic) statin acting as a prodrug, which needs to be converted in the liver into an open lactone form. These selections are not advocated by De Gasparo *et al.*

De Gasparo *et al.* does not give any preference to any particular combination within the broad disclosure, certainly not a specific combination of telmisartan and simvastatin. Indeed, De Gasparo *et al.*, at page 3, line 22, merely defines "AT_1 receptor antagonists" as including a number of commercially available sartans including telmisartan, which is not disclosed as a selected compound in the context of a specific combination, much less with simvastatin. The only sartan specifically mentioned in De Gasparo *et al.* in the context of a specific combination is valsartan which actually teaches away from telmisartan as a preferred combination partner. Similarly, in De Gasparo *et al.*, simvastatin is mentioned on page 5, lines 7 and 10, but not in the context of a specific combination, much less with telmisartan. On page 5, line 27, and page 6, line 1, De Gasparo *et al.* teaches that simvastatin is a preferred or most preferred composition partner with valsartan (not telmisartan), again teaching away from telmisartan as a preferred combination partner of simvastatin. Instead De Gasparo *et al.* on page 6, lines 8 and 11 refer to a combination of statins such as simvastatin with ACE inhibitors while there is no analogous teaching with regard to AT_1 receptor antagonists. The Examiner argues that this does not amount to a teaching away from the claimed invention, but applicants respectfully disagree if the full context is considered.

Furthermore, none of Robl *et al.*, Cecil's Textbook of Medicine, Harlan *et al.*, or Bohm *et al.* provide what De Gasparo *et al.* lacks in providing to one of skill in the art a motivation,

reasonable expectation of success, or teaching or suggestion of all of the claim limitations of the claimed invention.

First, Robl *et al.* does not teach structures which encompass simvastatin, does not teach combinations of simvastatin with any compound except for the class of HMG-CoA reductase inhibitors claimed, and does not mention telmisartan. Second, the teaching of Harlan *et al.* is confined to aerosol formulations of statins while said formulations are not intended to combine a statin such as simvastatin with an antihypertensive much less with telmisartan. Third, the teaching of Bohm *et al.* is confined to a combination of telmisartan with the ACE inhibitor ramipril, i.e., to two active ingredients acting on the renin-angiotensin system but not on HMG-CoA reductase. Fourth, Cecil's Textbook of Medicine neither mentions telmisartan nor simvastatin. Finally, neither De Gasparo *et al.*, Robl *et al.*, Cecil's Textbook of Medicine, Harlan *et al.*, nor Bohm *et al.* teach or suggest that telmisartan increases the expression of genes regulated by the PPARgamma receptor, i.e., an activity known from antidiabetic drugs, which is the reason that telmisartan is a preferred combination partner for simvastatin in the treatment of, e.g., diabetes, and this metabolic activity appears to be unique for telmisartan and is not recognized in the prior art. Indeed, De Gasparo *et al.* teaches the use of AT_1 receptor antagonists of "differing structural features" and therefore suggests that the specific chemical structure is of no concern and none of the other art cited makes up for this defect. Furthermore, neither Harlan *et al.* (disclosing an aerosol formulation of statins) nor Bohm *et al.* (disclosing a combination of telmisartan with ACE inhibitors) disclose, suggest, or hint at telmisartan combinations with statins and it is unclear why or how one of skill in the art at the time the claimed invention was made would combine their teachings with De Gasparo *et al.* Accordingly, applicants respectfully request that the Examiner reconsider and withdraw this rejection.

The Examiner also provisionally rejected claims 1 to 3 and 6 to 13 for nonstatutory obviousness-type double patenting over claims 1 to 13 of U.S.S.N. 11/560,059, in view of Frisbee *et al.*

In response, applicants undertake to file a terminal disclaimer with respect to U.S.S.N. 11/560,059, if (1) the instant claims be found otherwise allowable, and (2) applicants determine that such application poses a double patenting issue at that time. Since the scope

of the claims may change and moot the provisional rejection, there is not need to address this issue at this time. Accordingly, applicants respectfully request that the Examiner withdraw the provisional rejection for consideration later.

Applicants submit that all the pending claims are allowable and respectfully solicit a Notice of Allowance for all of the pending claims. If the Examiner feels that a telephone interview would be helpful in advancing prosecution of this application, the Examiner is invited to contact the attorney below.

Respectfully submitted,

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